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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,453	12/09/2004	Ogari Pacheco	4705-0106PUS1	5587

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
HUANG, GIGI GEORGIANA	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
01/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/517,453	PACHECO ET AL.	
	Examiner	Art Unit	
	GIGI HUANG	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,27,30,32-35 and 37-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-27, 30, 32-35, 37-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The response filed November 6, 2008 has been received, entered and carefully considered. The response affects the instant application accordingly:

   a. Claims 26 and 44 have been amended.

2. Claims 26-27, 30, 32-35, 37-45 are pending in the case.

3. Claims 26-27, 30, 32-35, 37-45 are present for examination.

4. The text of those sections of title 35.U.S. Code not included in this action can be found in the prior Office action.

5. All grounds not addressed in the action are withdrawn or moot.

6. New grounds of rejection are set forth in the current office action.

New Grounds of Rejection

7. Due to the amendment of the claims the new grounds of rejection are applied:

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 26-27and 30-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a method of making a ritonavir composition wherein the starting amount of the components (i.e. ritonavir, co-solvent, medium chain mono/diglycerides, antioxidants, stabilizer, polarity corrector) are defined by their final

amount at the end of the method in the final composition. It is unclear what the starting amounts are or how to ascertain what they should be based on a percentage of a resulting composition as the method will affect the amounts by several steps such as filtration of the particles (particularly the solid particles which as addressed by the specification is critical to guarantee the absence of solid particles to avoid precipitation which is known in the art to be an issue of the ritonavir and its polymorphs), as well as the distillation and reduction of the solution which directly affects the weight percentage and concentration. There is no example or formula presented in the specification to ascertain these starting amounts from a desired final amount. There is no means presented to utilize the *future percentages* to estimate the amount of material such as ritonavir to be used *during* the method of making as it does not address how much ritonavir (e.g. milligrams) is used during the method. Specifically, ritonavir is placed with an alcoholic solvent of C_2-C_4 (e.g. ethanol), dissolved, and *filtered-eliminating solid particles from the mixture* before proceeding with the incorporation of other components. As a result, the amounts used during the process are not the same as the final product and it is unclear how to ascertain the starting amount from the final amount. There is a general disclosure of the steps and examples of the final composition but not of the starting material amounts or ranges. As a result it is does not allow one of skill in the art to ascertain the metes and bounds of the invention.

For purposes of examination, any amount is acceptable.

10. Claims 26-27and 30-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a method of making a ritonavir composition with a final weight. However, the final weight is unclear and as the alcohol is use to correct to the final weight which is not cited. It does not allow one of skill in the art to ascertain the metes and bounds of the invention.

Response to Arguments

11. Claims 26-27, 30, 32-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicant's arguments filed 11/6/2008 have been fully considered but they are not persuasive. Applicant asserts that the weight percentages of the components are the same at the starting amount as in the final amounts as addressed by the examples. This is not persuasive as the examples cite the percentages of the final composition and not the starting amounts nor demonstrate the methods which are not commensurate in scope with the claims or the arguments. Secondly, the starting amounts cannot be the same as the final as the amount of ritonavir is affected first by the filtration process and Applicant's argument that the filtration is for microparticles as the ritonavir is completely dissolved, is a clear solution, and the solid particles removed not ritonavir is not persuasive as first, the ritonavir and the alcohol are mixed to form the solution which is clear but has solid particles which are filtered out as they can cause precipitation (see Page 17 lines 28-Page 18 line 20). The solution *only has ritonavir and the alcohol*,

which means the solid particles being removed *are from the ritonavir not in solution which affects the amount of ritonavir present in the final composition*. As for the assertion that the particles are microparticles or contaminants, the specification states the particles are solid which goes to a particle that is solid and large enough to be visually seen, and there is no disclosure of contaminants or the mesh size to support the assertion of microparticles.

Second, there is a reduction of the alcohol by 50%, addition of other components, and then removal of the alcohol which directly affects the concentration of the components in the final composition, and then the addition of alcohol as needed to correct the weight of the final composition where *no specific final weight is cited*. There is no description in the specification to describe the difference in concentration of the components at the start from the final. There is only a general disclosure of the steps and examples of the final composition but not of the starting material amounts or ranges. The reference to stability tables on Pages 36-37 are to the final product with do not address the issues present with written description of the instant claims and not commensurate in scope with the claims.

Accordingly, the rejection is maintained.

12. Claims 26-27, 30, 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments filed 11/6/2008 have been fully considered but they are not persuasive. Applicant's argument that the claims recite the final concentrations is

not persuasive as the starting amounts are stated in terms of what the final amounts should be, but it is unclear what the starting amounts are, it is also unclear what the final amounts are particularly as alcohol is used to correct the final weight but there no final weight stated at the end of the methods except a solution with 10-50% ritonavir but not an endpoint for the remaining components. This makes the claims indefinite as to what is the invention and leaves the metes and bounds of the claim unclear.

Accordingly, the rejection is maintained.

13. Claims 37-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipari et al. (U.S. Pat. # 6,232,333) in view of Bailey et al. (U.S. Pat. # 6,008,228).

Applicant's arguments filed 11/6/2008 have been fully considered but they are not persuasive. Applicant's argument that the arguments are to Bailey and that the closest prior art used in the previously submitted comparative is Bailey as it is to the medium chain mono/diglycerides and Applicant argues that the emphasis is to the glycerides and the process steps. This is not persuasive as process steps in a product claim as product by process limitations are viewed as product/composition claims by the office. The product with the closest composition to the instant invention is Lipari, not Bailey and in a product comparison, the comparison would be to the Lipari product as the composition components as a whole which would all be part of the invention.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was

within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. As Bailey teaches that there are known absorption and manufacturing problems with proteinase inhibitors because of the hydrophobic and /or lipophilic character of there inhibitors and that certain classes of glycerides used as carrier components can assist in alleviated these issues, particularly in achieving better absorptions and bioavailability, stability, and shelf life (Col. 1 line 66-Col.2 line 32) there is sufficient teaching by Bailey for one of skill of the art at the time of the invention to try and utilize these classes of glycerides as a carrier component for protein inhibitors for the taught improvements in absorption, bioavailability, stability, and shelf life. Applicant's argument in regards to the ranges of monoglycerides are not persuasive as routine experimentation and optimization in the art when the general conditions of a claim are disclosed in the prior art as Lipari teaches the general range for the organic solvent for the fatty acid to be from about 20% to about 99% (Col. 9 line 18-30) which would be substituted for the glyceride mixture and Bailey teaches that the mixture can be use from 0 %to 100% ((Col. 21 line 15-25) and the preferred range is about 40% to about 80% (Claim 1) which allows one of skill in the art to arrive at 20-40% through routine experimentation.

Accordingly, the rejection is maintained.

14. Claims 26-27, 30, 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipari in view of Bailey as applied to claims 37-45 above, and further in view of CUBoulder Organic Chemistry Undergraduate Courses, Lab Techniques.

Applicant's arguments filed 11/6/2008 have been fully considered but they are not persuasive. Applicant's arguments to complete dissolution and the issue of an endpoint and written description to the starting amounts are addressed above. As for the technique of vacuum distillation, it is a common and known technique for removing solvent, condensing, and purifying a compound (ritonavir). It is commonly used industrially and in laboratories commonly in the form of the rotary evaporator and would be obvious to one of skill in the art to use to distill any compound that might undergo decomposition on heating at atmospheric pressure, as it is used with or without heat, and used to remove solvents from the mixture without damaging the product if desired The arguments to the polymorphic forms is not persuasive as the filtration process taught by the art as removes the insoluble particles are removed from the solution, and they are not commensurate in scope with the claims as the instant claims removes the insoluble particles from the solution as addressed above, and the comparative is to the Bailey reference not Lipari as addressed above.

The rejection is maintained.

Conclusion

15. Claims 26-27, 30, 32-35, 37-45 are rejected.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH
/Zohreh A Fay/
Primary Examiner, Art Unit 1612